THE ROLE OF ALPHA-ADRENERGIC AGONISTS IN THE MYOCARDIAL ISCHEMIA PREVENTION

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The ischemia is one of the most fearsome events in the medicine. The lack of oxygen leads to irreversible tissue damages, wherever it happens. When the affected tissue is the myocardial, the lesion is quite severe due to the importance of the heart to the physiological normality.

In anesthetized patients, myocardial oxygen requirements may increase beyond expected due to surgical stress (1, 2). In spite of been anesthetized the body understands the surgery as an aggression and it releases adrenaline. Whenever the person is attacked, the autonomous nervous system reacts immediately and one of the side effects in this situation can be ischemia.

It is well established that an imbalance of the autonomic nervous system can be involved in the genesis of the myocardial ischemia. Such events can have its pathophysiological mechanism originated in the activation of the sympathetic central nervous system. The increase of the sympathetic activity may result in ischemic events of the myocardial layer due to the myocardial electric instability (3, 4).

The stress, mediated by the sympathetic system, is one of the worst surgical factors, because it can activates the endocrine system and releases nor-epinephrine until two days after surgery. Nor-epinephrine increases consumption of oxygen and glucose, reducing the organic defenses. Such a body behavior comes before, during and after surgery.

This cascade of events can be avoided preoperatively. Many drugs as opioids, cardiac blockers, among others, have been used in order to modulate sympathetic tone. The Sympathetic hyperactivity may be modulated by drugs acting directly on its site of origin in the central nervous system. Recently the alfa-2 adrenergic agonists have been used with the purpose of preventing myocardial ischemia, because of its possibility of controlling sympathetic nervous system discharges. The ability of alpha-2 adrenoceptor agonists to inhibit central sympathetic outflow

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may benefit patients with risk of myocardial damage by improve the myocardial oxygen demand and supply ratio (5, 6).

Among these new agents, clonidine, first generation centrally acting drugs, showed a better ability to inhibit central sympathetic outflow, improve myocardial oxygen demand and supply ratio and also have a role in providing haemodynamic stability. Clonidine, a central alpha-adrenoceptor agonist, decreases sympathetic outflow, increases parasympathetic tone, decreases the rennin - angiotensin system activity and decreases vasopressin blood concentration (7- 9). As a result, systemic arterial blood pressure is lowered, resting heart rate is decreased and exercise-induced tachycardia is attenuated (10). Decrease in systemic arterial pressure and systemic vascular resistance leads to a lowered myocardial wall tension (14). Clonidine also has the capacity of modify the pain perception, which contributes to decrease oxygen consumption. These effects would theoretically contribute to avoid or minimize the effects of myocardial ischemic events (11).

The alpha-2 adrenoceptor agonist, clonidine, can act directly in the central nervous system, in sites of nor-epinephrine release as the locus ceruleus. This is a tiny nucleus located in the brainstem at the level of the fourth ventricle. In the human brain, it is readily identifiable because of its bluish color, caused by melanin pigments (12). This brain nucleus attracted intense interest in the last two decades, largely because of its relationship with emotional behavior. Many evidences pointed this brain nucleus taking a role in emotional behavior such as wakefulness, depression, dementia of the Alzheimer type and, consequently, stress. There is, perhaps, more knowledge about the anatomical projections and postsynaptic effects of the locus ceruleus than any other system in brain due to the interest that wakes up about the stress mechanism. Recent studies with radioisotopes have also revealed a homogenous set of discharge properties from its cells and shown that specific behavioral and sensory events evoke concerted activity of its neurons (13). The observed data lead to the suggestion that wakefulness is controlled by this nucleus and that, clearly, this would have important implications for clinical anesthetic practice (12).

Clonidine and others alpha-2 adrenergic agonists such as dexmedetomidine can act directly in locus ceruleus decreasing or avoiding the nor-epinephrine release. Administration of this drug, that is 200 times specific for the alpha-2 receptors, reduced the incidence of perioperative myocardial ischemic episodes from 39% to 24% (6). Reduction in frequency of coronary pains by at least 50% was observed in chronic anginous patients (14). and a big decrease in ST-segment elevation was observed: after 24 hr (37% of initial value) and after 48 hr (30%) measured by precordial electrocardiografic mapping (15). Clonidine was effective in reducing the exercise-induced increases in blood pressure (20.8%) and the effort related ventricular extra

systoles were reduced by greater than 50%. In patients who had been diagnosed with coronary artery disease or who had at least two of the following five risk factors for cardiac disease: aged 60 years or older, hypertension, smoking within one year, cholesterol of 240 mg/dL or more, or diabetes submitted a noncardiac surgery; the mortality decreases 50% at two years (16).

Finally, the results show that clonidine present cardioprotective effect and that a small oral dose, given prophylactically, can reduce the incidence of perioperative myocardial ischemic episodes without affecting hemodynamic stability, even in patients with documented coronary artery disease (5).

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